U.S. SMALL BUSINESS ADMINISTRATION
WASHINGTON, D.C. 20416

OFFICE OF CHIEF COUNSEL FOR ADVOCACY

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Dockets Management Branch (HFA-305)
Food & Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Small Business Impact Relating to the International Drug Scheduling of Ephedrine, Dihyroetorphine, Remifentanil, and Certain Isomers; 64 Fed. Reg. 1629 (January 11, 1999); Docket No. 98N-0148.

Dear Sir or Madam:

The Office of the Chief Counsel for Advocacy of the U.S. Small Business Administration was created in 1976 to represent the views and interests of small businesses in federal policy making activities.[1] The Chief Counsel participates in rulemakings *and other federal agency actions* when he deems it necessary to ensure proper representation of small business interests. In addition to these responsibilities, the Chief Counsel monitors agencies' compliance with the Regulatory Flexibility Act (RFA),[2] and works with federal agencies to ensure that their rulemakings demonstrate an analysis of the impact that their decisions will have on small businesses.

The above-referenced Food and Drug Administration (FDA) notice solicits comments on the World Health Organization's (WHO) recommendation to place ephedrine in Schedule IV of the Convention of Psychotropic Substances of 1971. Inasmuch as FDA will prepare the U.S. position on the recommendations for an upcoming meeting of the United Nations Commission on Narcotic Drugs (CND), the Office of Advocacy wishes to provide information on the potentially significant small business impacts of supporting the WHO's recommendation.

Unless a special exemption is created, the international scheduling of ephedrine will have the effect of eliminating the over-the-counter (OTC) status that the chemical/drug currently has. The OTC products have been used safely and effectively for at least 40 years by consumers who desire the option of self-treatment for mild symptoms resulting from colds, asthma, bronchitis, etc. Without OTC status, the products will be available by prescription only. Such a result is bad for consumers and small businesses.

Although it appears that most bronchodilator products containing the pharmaceutical chemical ephedrine and most dietary supplements containing extracts of the herb Ephedra

[1] Pub. L. No. 94-305 (codified as amended at 15 U.S.C. §§ 634a-g, 637).
[2] Pub. L. No. 96-354, 94 Stat. 1164 (1980) (to be codified as amended at 5 U.S.C. §§ 601-612)

98N-0148

C 32

are manufactured by small businesses, the bulk of OTC retail sales probably go to large businesses (i.e., manufacturers of brand name products like Sudafed™).[3] This discrepancy will become more pronounced when the drugs/dietary supplements become available only by prescription. Physicians will write prescriptions for the more well known brand names, leaving many smaller manufacturers out of the loop. However, the more dramatic impact is likely to be with the Ephedra manufacturers that will no longer have a market for their products if placed in direct competition with ephedrine and placed in Schedule IV of the 1971 Convention. The scheduling of these substances will also have a ripple effect throughout the distribution network for Ephedra—a network comprised of thousands of home-based and otherwise small distributors.

Having to visit the doctor for a prescription to treat occasional mild asthma attacks is more than a mere inconvenience for consumers who require the products. For those consumers (possibly millions) without health insurance or prescription drug coverage, the drugs may become inaccessible or too expensive. Moreover, even for consumers with prescription drug coverage, dietary supplements typically are not included in that coverage. In any event, it is highly unlikely that physicians will write prescriptions for herbal-based dietary supplements when major brand name chemical mixtures are available.

The effort to schedule ephedrine is based on a desire by the WHO to halt alleged worldwide abuse. In fact, one of the requirements of the 1971 convention is that **sufficient** evidence of abuse or potential abuse must exist in order to schedule a chemical.[4] Although the Office of Advocacy has not had the opportunity to review the WHO's justification and supporting information for the proposed action,[5] Advocacy is not aware of any significant measurable evidence that exists in the U.S. relating to actual abuse. It seems that the WHO's action is based on a general concern for potential abuse and, to a certain degree, on possibly confusing documentation supplied by the FDA Frankly, there seems to be no compelling government interest or factual basis for effecting such a harmful policy.

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[3] This conclusion is based on an extrapolation using general industry data for all pharmaceuticals and botanicals. The data are produced by the Bureau of the Census and the Office of Advocacy and is based on the 4-digit Standard Industrial Classification (SIC) codes for Medicinal Chemicals & Botanicals (SIC 2833) and for Pharmaceutical Preparations (SIC 2834). The data show that for medicinal chemicals and botanical products (including ephedrine and derivatives), 88% of the industry has fewer than 500 employees, but has only 23% of the annual receipts. For pharmaceutical preparations (including cold remedies), 86% of the industry has fewer than 500 employees, but has only 12% of the annual receipts. SBA's definition of a small business in these industries is one with 750 or fewer employees. *See* 13 C.F.R. § 121.201. Although SBA has data on the total number of businesses in an industry, the data is not broken down in increments when the number of employees exceeds 500. Therefore, SBA does not have specific data based on the 750-employee standard.

[4] *See* 1971 Convention, art. 2, para. 4.

[5] The supporting documents were not part of the published notice of January 11, 1999 and the comment period is unusually brief given the potential impact and significance of the proposed action. In addition, it bears noting that FDA's published notice appeared in the *Federal Register* one week after the deadline for submitting comments from the U.S. to the UN Commission on Narcotic Drugs (UNCND). The opportunity for meaningful comment and the likelihood that comments received will be considered seriously seem remote.

FDA's notice contained formal UN notifications that "explain the basis for the recommendations." To substantiate its claims of actual abuse and/or evidence of the potential abuse, the WHO indicated that "[t]he current problem of abuse seems to be particularly serious in certain African countries...[however, w]hen abuse exists, it seems to involve ephedrine single entity products." The WHO goes on to say, "in the USA, combination products containing ephedrine in herbal preparations have been abused." This is a curious statement because the existence of such abuse in the USA has not been clearly established.

The Office of Advocacy has spent a great deal of time and effort analyzing FDA's 1997 proposed rule on dietary supplements containing ephedrine alkaloids.[6] This proposed rule and its supporting record seem to form the basis of the WHO's assessment regarding abuse of combination products in the USA. Yet, the proposed rule, its analytical methodology and its unsubstantiated claims regarding safety (not abuse) have been called into question by the Office of Advocacy and others. The General Accounting Office is currently preparing a report about, among other things, the formulas used to calculate the impact of the proposed rule and the lack of reliable science/data in the proposed rule. The proposed rule has been the subject of meetings at the Office of Management and Budget and has also generated questions by members of Congress. In fact, FDA conceded in its own rulemaking that their database (consisting of adverse event reports) was unreliable. Submitting unreliable information to the WHO (that is primarily focused on safety concerns and not abuse) lends itself to misinterpretation and misapplication—the apparent results here.

This effort to schedule ephedrine comes at a very unique and opportune time for FDA. It comes at a time when both FDA and the Drug Enforcement Administration (DEA) have rules pending that attempt to regulate ephedrine-containing products based on alleged safety concerns and diversion prevention. If the effort to schedule ephedrine is successful, the two agencies no longer have to worry about going through the motions of the rulemaking process for any of the pending rules.

The Office of Advocacy urges FDA to oppose **vigorously** any effort to place ephedrine or ephedrine alkaloids in Schedule IV of the 1971 Convention. The impact on the US economy and small businesses could reach into the billions of dollars. The impact on consumers who need these products is incalculable. This major policy initiative requires a great deal of study and analysis, therefore, the Office of Advocacy would like to reserve the right to make further comments on this issue pending a full revue of FDA's docket. Please do not hesitate to contact my office if you have any questions concerning these comments, 202-205-6933.

Sincerely,

Jere W. Glover
Chief Counsel for Advocacy

Shawne Carter McGibbon
Asst. Chief Counsel for Advocacy

[6] 62 Fed. Reg. 30,678 (June 4, 1997).